
Solvent Effects: 6. A Comparison between Gas Phase and Solution Acidities

KENNETH B. WIBERG* and HENRY CASTEJON

Department of Chemistry, Yale University, New Haven, Connecticut 06520

TODD A. KEITH

Lorentzian Inc., 140 Washington Avenue, North Haven, Connecticut 06473

Received 10 January 1995; accepted 18 April 1995

ABSTRACT

A new *ab initio* reaction field model has been applied to the calculation of the change in free energy of ionization on going from the gas phase to dimethylsulfoxide solution for a series of weak organic acids. In most cases, the observed change in free energy is reproduced within the experimental uncertainty of the gas phase experimental data. © 1996 by John Wiley & Sons, Inc.

Introduction

In recent years, a large body of gas phase acidity data has become available.¹ There remains the challenge of relating the gas phase acidities to those measured in solution, and this requires information on the heats of solution of an acid, its anion, and the proton. A valuable theoretical approach has been to use Monte Carlo statistical mechanics with explicit representation of the solvent to compute the necessary free energy changes and relative pK_a 's.² Continuum models of the solvent have also been used for pK_a calculations

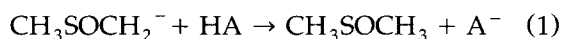
through classical electrostatic and Poisson-Boltzmann approaches.³ However, these procedures all require values of charges at the atoms being considered, and there is still a question concerning how best to obtain these charges.⁴ In addition, the charge distribution in the solute is not allowed to relax on going to a medium of high dielectric constant. An alternate approach is to use reaction field theory in the context of *ab initio* molecular orbital (MO) calculations.⁵⁻⁸ Here, the only quantities, beside the choice of basis set and theoretical level, are the volume of the solute and the dielectric constant of the solvent.

It is now possible to make good estimates of the relative heats of solution of compounds in solvents that do not give specific solvent effects by using a

*Author to whom all correspondence should be addressed.

recently developed reaction field model.⁹ This model has not been tested for ionic species, and we now wish to see if it is also successful in treating these cases. Acidities provide the largest body of experimental data with which the theoretical calculations may be compared.

Bordwell has measured the acidities of a large body of acids in dimethyl sulfoxide as the solvents.¹⁰ This is a useful solvent for the present purpose because it eliminates the problems associated with hydrogen bonding. We do not wish to calculate the acidities directly, since this requires one to account correctly for the heat of solution of a proton, a quantity which is difficult to obtain either theoretically or experimentally. Thus we shall examine proton transfer reactions such as the following:



The gas phase free energy of ionization of dimethyl sulfoxide has been found to be 366 ± 2 kcal/mol, and making use of this value, all of the available gas phase data¹ may be obtained relative to dimethyl sulfoxide (DMSO). Some typical data are shown in Table I. The energy changes for the selected compounds cover a range of 32 kcal/mol.

The solution phase $\text{p}K_a$ values may be treated in the same fashion, taking the $\text{p}K_a$ of DMSO in DMSO as 35. The solution free energies of ionization have been conveniently summarized by Taft and Bordwell making use of 9-phenylfluorene as the reference compound.¹ This was not useful for our purpose since *ab initio* calculations on such a large molecule are not practical at this time, so the values were shifted to be relative to DMSO. The final column of Table I gives the change on going from the gas phase to DMSO solution. Is it possi-

ble to reproduce these data using a reaction field model?

Before considering the computational results, the $\Delta\Delta G$ values deserve some comment. The largest $\Delta\Delta G$ values are found with the alcohols that give fairly localized charges on the electronegative oxygens. When the charge is distributed over two oxygens, as in the anions from acetic acid or nitromethane, the $\Delta\Delta G$ values are reduced by a factor of about 2. One might reasonably expect that localized charges would be better stabilized by polar solvent than are charges distributed over two or more atoms. It is less clear why the anions from dimethylsulfoxide and sulfone experience the smallest solvent effect, and this continues to be studied.

Computational Method

The solvation free energies reported herein were calculated using a new self-consistent reaction field (SCRF) model based on the Tomasi polarizable continuum (PC) model.⁶ In this model, a solute molecule is placed in a cavity within the solvent, which is treated as a simple dielectric characterized by its bulk dielectric constant (ϵ). The electric field \vec{E}_0 from the solute charge distribution induces a dipole density distribution \mathbf{P} within the solvent:

$$\mathbf{P}(\mathbf{r}) = (1 - \epsilon)\vec{E}(\mathbf{r}) = (1 - \epsilon)(\vec{E}_0(\mathbf{r}) + \vec{E}_p(\mathbf{r}))$$

where $\vec{E}(\mathbf{r})$ is the total electric field at point \mathbf{r} in the solvent, including that from \mathbf{P} itself, $\vec{E}_p(\mathbf{r})$.

Taking advantage of Gauss's law, the potential from solvent polarization appears in the solute

TABLE I.
Relative Experimental Free Energies of Ionization in the Gas Phase and in DMSO Solution, kcal/mol.^a

Compound	$\Delta G(\text{gas})$	$\Delta\Delta G(\text{gas})$	$\Delta\Delta G(\text{DMSO})$	$\Delta\Delta G(\text{gas} \rightarrow \text{DMSO})$
Acetic acid	342 ± 2	-24	-32	-8
Nitromethane	350 ± 2	-16	-24	-8
Dimethyl sulfone	358 ± 2	-8	-5	3
Acetone	362 ± 2	-4	-12	-8
1-Butyne	362 ± 2	-4	-9	-5
Acetonitrile	365 ± 2	-1	-5	-4
Dimethyl sulfoxide	366 ± 2	0	0	0
Ethanol	371 ± 2	5	-7	-12
Methanol	374 ± 2	8	-8	-16

^aThe ΔG values for the gas phase were taken from ref. 1 except for 1-butyne, which was taken from ref. 11. The ΔG values for DMSO solution were taken from ref. 11.

Hamiltonian \hat{H} in terms of a distribution of charge density, σ_p , over the solute cavity surface. At a point \mathbf{r}_s on the cavity, surface σ_p is given by

$$\begin{aligned}\sigma_p(\mathbf{r}_s) &= -[(\epsilon - 1)/4\pi\epsilon] \vec{E}(\mathbf{r}_s) \cdot \hat{n}(\mathbf{r}_s) \\ &= -[(\epsilon - 1)/4\pi\epsilon] \left[\left(\vec{E}_0(\mathbf{r}_s) + \vec{E}_p(\mathbf{r}_s) \right) \cdot \hat{n}(\mathbf{r}_s) \right]\end{aligned}$$

where $\hat{n}(\mathbf{r}_s)$ is the outward normal vector at \mathbf{r}_s . The

solute Hamiltonian in solution is given by

$$\hat{H} = \hat{H}^{(0)} - \sum_i \phi \frac{\sigma_p(\mathbf{r}_s) d\mathbf{r}_s}{|\mathbf{r}_i - \mathbf{r}_s|} + \sum_n Z_n \phi \frac{\sigma_p(\mathbf{r}_s) d\mathbf{r}_s}{|\mathbf{R}_n - \mathbf{r}_s|}$$

where $\hat{H}^{(0)}$ is the corresponding gas phase Hamiltonian, the first summation is the operator for the interaction between electrons and the solvent, and the second summation is the operator for the interaction between the nuclei and the solvent.

TABLE II.
Calculated Energies for the Gas Phase.

a. Total energies (Hartrees). For each entry, the parent compound is given on the first line and its anion is given on the second line.

Compound	ZPE ^a	MP2 / 6-31 + G*	MP2 / 6-311 + + G**	G2(MP2)
Acetic acid	37.4	-228.43573	-228.56788	-228.74757
	29.1	-227.88285	-228.00200	-228.20285
Nitromethane	30.5	-244.35176	-244.47809	-244.67216
	22.1	-243.77268	-243.89060	-244.09905
Acetaldehyde	33.6	-153.35801	-153.44932	-153.57297
	25.4	-152.76474	-152.85083	-152.98939
Dimethylsulfone	51.5	-627.17444	-627.33733	
	42.7	-626.57759	-626.73765	
Acetone	50.3	-192.53670	-192.65540	
	42.2	-191.93877	-192.05308	
1-Butyne	50.1	-155.39551	-155.49061	-155.62158
	43.3	-154.80355	-154.89377	-155.03522
Acetonitrile	27.3	-132.34536	-132.41102	-132.51984
	18.1	-131.73674	-131.79906	-131.92514
Dimethylsulfoxide	48.0	-552.13005	-552.26291	
	39.4	-551.52119	-551.65065	
Ethanol	48.1	-154.53015	-154.64531	
	38.9	-153.92273	-154.02726	
Methanol	30.9	-115.35784	-115.44495	-115.53282
	21.6	-114.74453	-114.82010	-114.92442

^aBased on HF / 6-31 + G* frequency calculations scaled by 0.893. The units are kcal/mol. The G2(MP2) energies include the zero-point energies.

b. Gas phase enthalpies of ionization, kcal/mol.

Compound	MP2 / 6-31 + G*	MP2 / 6-311 + + G**	G2(MP2)	Obs. ^b
Acetic acid	338.7	347.0	346.1	348 ± 3
Nitromethane	355.0	360.3	359.6	355 ± 3
Acetaldehyde	364.1	367.4	366.2	365 ± 3
Dimethylsulfone	365.7	367.5		366 ± 3
Acetone	367.2	370.0		369 ± 3
1-Butyne	364.7	367.0	367.9	369 ± 3 ^c
Acetonitrile	372.7	374.8	373.2	372 ± 3
Dimethylsulfoxide	373.5	375.6		374 ± 3
Ethanol	372.0	378.7		376 ± 3
Methanol	375.6	382.8	381.8	379 ± 3

^bSee ref. 1.

^cBased on ΔG from ref. 11 and correction to ΔH .

The solute wave function Ψ and the energy E are thus modified in the presence of the solvent. Since \hat{H} depends on the solute wave function (via \vec{E}_0), proper application of a PC model must lead to self-consistency (SCRF) between Ψ and \mathbf{P} . The (electrostatic) solvation free energy ΔG_{sol} within a PC model is given by the difference between the expectation value of the solute Hamiltonian in solution, E , and in the gas phase, $E^{(0)}$, plus the free energy required to polarize the solvent, E_{pol} , which is assumed to be minus one-half of the interaction energy between the solvent and solute.⁶

For general solute charge distributions and/or general cavity shapes, the potential integrals from σ must be calculated numerically (i.e., as a sum of contributions from a finite number of points on the cavity surface each with an appropriate position and weight). The solute electronic contribution of σ_p at the relatively large number of surface grid points (typically ~ 4000) is calculated efficiently using the PRISM algorithm.¹² The calculations may be efficiently carried out at the RHF, MP2, QCISD, and DFT levels of theory. As an example, RHF energy calculations require only 20 to 50% more computer time than the standard gas phase calculations.

We have chosen to define the solute cavity explicitly in terms of a property of the solute, an isosurface of its electron distribution, which is generally considered to provide a reasonable definition of "molecular shape." We have found that the molar volumes defined by the 0.0004-au isosurface are in good correspondence with the experimentally measured liquid molar volumes. For example, the calculated molar volumes of acetonitrile, acetaldehyde, and ethanol are 52.6, 53.3, and 58.9

mL and the observed volumes are 52.2, 54.7, and 58.4 mL, respectively.

There are some difficulties associated with the accurate evaluation of the potential and electric field integrals arising from the surface charge distribution, σ_p , especially at points on the surface itself. They have been overcome in this work, and the accuracy of the integrals is not a limiting factor in this model. The details of our implementation will be described in detail in a separate publication.⁹

Results and Discussion

The structures of the compounds and ions in this study were obtained by geometry optimization at the MP2/6-31 + G* theoretical level using Gaussian 93.¹³ This is known to give good structural parameters¹⁴ and includes diffuse functions that are important in describing anions.¹⁵ The energies calculated at the MP2/6-31 + G* level for the acids and their anions in the gas phase are summarized in Table II. To see the effect of using a more flexible basis set, the energies also were calculated at the MP2/6-311 + G** level using the MP2/6-31 + G* geometries. In some cases, the G2(MP2)¹⁶ energies also were available,¹⁷ and they are included in the table. This level of theory is effectively QCISD(T)/6-311 + G(3df, 2p) plus corrections for zero-point energies and a higher-level term. The gas phase acidities calculated from these energies are summarized in the second part of Table II and are compared with the gas phase enthalpies of ionization. With most of the compounds, all three theoretical levels give energies

TABLE III.
Calculated Solvents Effects, MP2 / 6-31 + G* Energies at $\epsilon = 40$.^a

Compound	Acid	Anion	$\Delta E(\text{soln})$	ΔG_{el}
Acetic acid	-228.44363	-227.97887	283.4	55.3
Nitromethane	-244.35868	-243.86726	300.0	55.0
Dimethylsulfone	-627.18757	-626.66661	318.1	47.6
Acetone	-192.54223	-192.02796	314.7	52.5
1-Butyne	-155.39823	-154.89644	308.1	56.6
Acetonitrile	-132.35242	-131.82344	322.7	50.0
Dimethylsulfoxide	-552.14143	-551.60761	326.4	47.1
Ethanol	-154.53669	-154.02140	314.2	57.8
Methanol	-115.36455	-114.84915	314.1	61.6

^a The total energies are given in Hartrees and the relative energies are given in kcal / mol.

that agree with experiment, and the MP2/6-31 + G* level is satisfactory. With the compounds having hydroxy groups (acetic acid, ethanol, and methanol) the smaller basis set underestimates the enthalpies of ionization. However, it should still be satisfactory for calculating the change in energy on going from the gas phase to solution.

The solvent effects were calculated at the MP2/6-31 + G* level using the gas phase structures and a dielectric constant of 40, which is close to that of DMSO. The energies are given in Table III. The calculated energy changes for reaction 1 are given in Table IV.

The solvation free energies should be corrected for the change in energies of creating the cavities in the solvents for the acid and the anion, and this was estimated using Pierotti's method.¹⁸ The final corrected relative free energies are compared with the experimental values in Table IV. The calculated free energy changes generally agree with the observed values with their uncertainties (~ 3 kcal/mol).

In the calculations, the charge distribution was allowed to relax in the presence of the polar medium, but the geometry was kept at the gas phase geometry. We are developing a procedure within this model for carryout out geometry optimization in the presence of a solvent,¹⁹ and in the future it will be applied to the molecules in this study. The extension to other compounds and solvents is also under investigation.

Acknowledgment

This investigation was supported by the National Science Foundation and Lorentzian Inc.

TABLE IV.
Calculated Free Energy Changes, kcal/mol.

Compound	$\Delta G(\text{el})$	$\Delta G(\text{cavity})$	$\Delta G(\text{total})$	$\Delta \Delta G(\text{gas} \rightarrow \text{DMSO})$	
				Cal.	Obs. ^a
Dimethyl sulfone	-47.6	1.3	-46.3	-1	3
Dimethyl sulfoxide	-47.1	1.5	-45.6	0	0
Acetonitrile	-50.0	1.7	-48.3	-3	-4
Acetone	-52.5	1.5	-51.0	-5	-8
1-Butyne	-56.6	1.8	-54.8	-9	-5
Nitromethane	-55.0	1.1	-53.9	-8	-8
Acetic acid	-55.3	1.0	-54.3	-9	-8
Ethanol	-57.8	1.4	-56.4	-11	-12
Methanol	-61.2	0.3	-60.9	-15	-16

^aThe uncertainty in the observed values is about ± 3 kcal/mol.

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